

**REMARKS**

Claims 2-7 are pending in the present application and are rejected. Applicants' representative thanks the Examiner for the courtesies extended in the personal interview of February 26, 2007. Applicants' response to the comments contained in the Interview Summary is incorporated herein.

**Applicants' Response to Claim Rejections under 35 U.S.C. §102**

**Claims 1, 2, 4, and 5 were rejected under 35 U.S.C. §102(b) as being anticipated by Chee et al. (U.S. Patent No. 6,429,027).**

It is the position of the Office Action that Chee discloses the invention as claimed. Chee is directed at composite arrays utilizing microspheres, as generally illustrated in Figures 1A and 1B. These "microspheres," "particles" or "beads," are bound to a substrate in an array, as described at column 17, lines 31-62. The microspheres may be bound to the substrate randomly or non-randomly. These beads may have a bioactive agent such as DNA or RNA bound to them. The beads may also have bound to them "identifier binding ligands" (IBL). Each IBL has a specific "decoder binding ligand" (DBL) which it may bind to. These IBL/DBL combinations may be antigen-antibody or other materials. According to Chee, "the DBL may be attached to a bead, i.e. a "decoder bead," that may carry a label such as a fluorophore." Column 15, lines 51-53.

In the Personal Interview of February 26, 2007, Applicants' representative and the Examiner discussed the Chee reference, and its many embodiments. It is the position of the

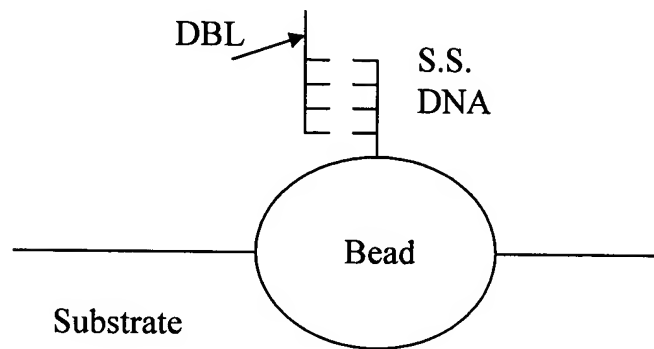
Office Action that the IBL/DBL combination is analogous to the antigen-antibody reaction of the present invention. Additionally, in the pending Office Action it is stated that “[w]hile Chee teaches that the DBL may be attached to a bead, this is a substrate encompassed within the claims.” However, in the interview, it was established that it is the *IBL* which is bound to the bead and thus to the substrate. As discussed below, the *DBL* may optionally be bound to a fluorescent bead. Based on the substance of the interview and further consideration of the references, Applicants herein present the following comments.

Applicants herein summarize the relevant embodiments of Chee. First, Applicants note that Chee discloses *two types of beads*. The first is a “bead” or “microsphere” which is attached to the substrate by, for example, “photoactivatable attachment linkers or photoactivatable adhesives or masks.” See column 17, lines 51-62. This is the “bead” discussed throughout the disclosure of Chee. Additionally, Chee discloses a second bead, which is a “decoder bead” bound to a DBL. See column 15, lines 51-53. Although Chee discloses the use of the first “bead” in nearly all embodiments, it is possible to omit this bead, and attach bioactive agents directly to a substrate. See column 4, lines 45-49.

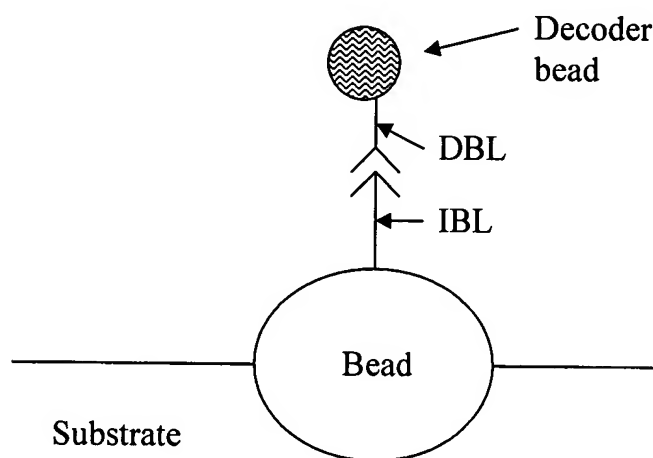
In a relevant embodiment of Chee, a single-stranded nucleic acid may be bound to the beads. Although not directly relevant to the rejection, Applicants discuss this embodiment for explanatory purposes. The DBL may then bind directly to the bioactive agent, which is a single-stranded nucleic acid. No IBL is used. Such an embodiment is illustrated in the simplified explanatory diagram below. This embodiment is discussed for example at column 5, lines 34-36 and 58-62; and column 13, lines 38-40. However, because this DBL/nucleic acid interaction is

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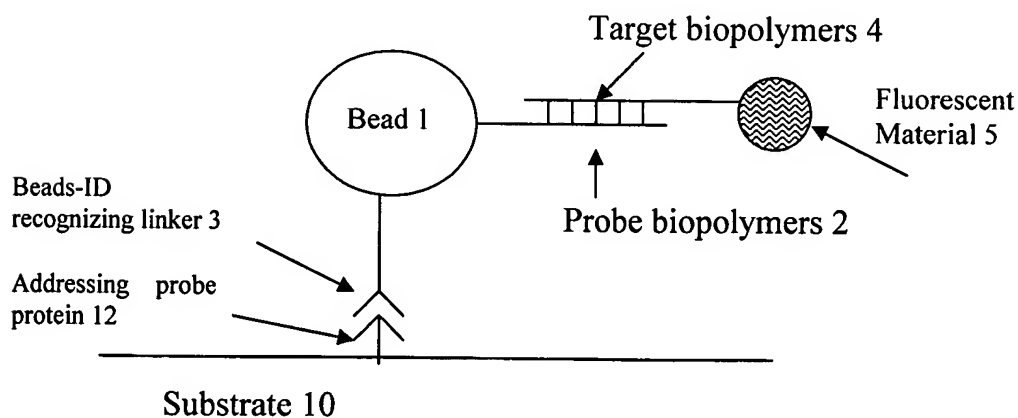
not an antigen-antibody pair, such an embodiment does not anticipate the claimed invention. Additionally, as noted above, the “bead” is optional and the single stranded DNA may be bound directly to the substrate.



Next, Applicants discuss the embodiment upon which the rejection relies. In this embodiment, Chee discloses the use of an IBL/DBL pair. See column 5, lines 33-36. The IBL/DBL pair may be complementary single-stranded nucleic acids. See column 15, lines 54-55. Alternatively, the IBL/DBL pair may be an antigen/antibody pair. Column 15, line 23. One or more IBLs are attached to the bead. See column 16, lines 36-55. The DBL may optionally be attached to a fluorescent bead. See column 15, lines 51-53. Such an embodiment is illustrated in the simplified explanatory diagram below. Additionally, as above, the “bead” is optional, and the IBL may be bound directly to the substrate.



On the other hand, in the present invention, an antibody-antigen reaction acts to bind addressing probe protein 12, which is attached to the substrate 10, and address linker 3, which is attached to bead 1. Specifically, proposed new claim 7 recites “capturing said beads-ID recognizing address linkers fixed to said beads by an antigen-antibody reaction using an addressing probe protein fixed to a substrate.” In other words, the bead 1 is bound to the substrate 10 via a specific antigen-antibody reaction. This is illustrated in the simplified diagram below.



In view of the above comments, Applicants respectfully submit that Chee does not disclose or suggest the method as claimed. It appears that the Examiner may be erroneously combining several features of Chee. While Chee may disclose a “bead” with a nucleic acid attached (See page 4, *supra*), a “bead” with an IBL attached (See page 5, *supra*), a “decoder

bead” with a DBL attached (See page 5, *supra*), and a nucleic acid with a DBL attached (See page 4, *supra*), it does not disclose these simultaneously. In particular, Applicants note that Chee does not disclose a step of “fixing probe biopolymers and beads-ID recognizing address linkers onto the surface of the beads.” In other words, the present invention requires that *two elements* are fixed on to the bead. A first element is the probe biopolymers 2, and a second element is the beads-ID recognizing linker 3. The bead is then put in a solution to hybridize the target polymers and probe polymers. Then, the solution containing the beads is poured onto the addressing probe protein to capture beads on the addressing protein sites. The beads-ID recognizing linker 3 is attached to the substrate by an antibody/antigen reaction. As this time, the addressing is performed by the arrangement of the addressing probe protein. Chee does not disclose such a construction. While Chee uses the IBL/DBL combination to connect a label, the present invention uses the antigen/antibody reaction in addressing of a specific position.

In the personal interview, the Examiner was of the position that the “decoder” bead was fixed to the substrate via an antibody/antigen reaction, and thus Chee anticipated the present invention. The Examiner broadly interpreted the IBL as being “fixed” on a substrate, despite the presence of a “bead” in the preferred embodiment. Applicants respectfully submit that while Chee may be broadly interpreted to disclose a fluorescent “decoder bead” attached to a substrate via an antigen/antibody pair, Chee does not disclose the invention as claimed.

The “bead” of Chee is not analogous to the bead 3 of the present invention. This is because the claims require that the bead 3 is linked to the substrate via an antigen/antibody reaction. On the other hand, the “bead” of Chee is attached to the substrate by using

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“photoactivatable attachment linkers or photoactivatable adhesives or masks.” Additionally, the “decoder bead” of Chee is not analogous to the bead 3 of the present invention. Although the “decoder bead” of Chee may be attached to the substrate via an antibody/antigen reaction, it does not have both a “probe biopolymer” and “beads-ID recognizing address linker” fixed to its surface. Therefore, Applicants respectfully submit that for at least the foregoing reasons, Chee does not disclose or suggest the invention as claimed.

**Applicants’ Response to Claim Rejections under 35 U.S.C. §103**

**Claim 3 was rejected under 35 U.S.C. §103(a) as being unpatentable over Chee in view of Collier et al. (U.S. Patent No. 5,985,548).**

It is the position of the Office Action that Chee discloses the invention as claimed, with the exception of teaching a method of stirring beads. The Office Action relies on Collier to provide this teaching. Collier discloses that “[t]est mixtures are agitated to assure contact with the bead supports.” See column 30, lines 11-12. The Office Action regards this passage as teaching stirring steps to ensure contact of beads and nucleic acids. In response, Applicants respectfully submit that claim 3 is patentable due to its dependency on claim 7, which Applicants submit is patentable for at least the reasons discussed above.

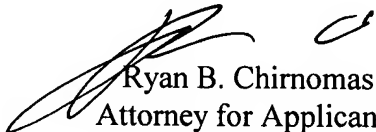
For at least the foregoing reasons, the claimed invention distinguishes over the cited art and defines patentable subject matter. Favorable reconsideration is earnestly solicited.

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Should the Examiner deem that any further action by applicants would be desirable to place the application in condition for allowance, the Examiner is encouraged to telephone applicants' undersigned attorney.

If this paper is not timely filed, Applicants respectfully petition for an appropriate extension of time. The fees for such an extension or any other fees that may be due with respect to this paper may be charged to Deposit Account No. 50-2866.

Respectfully submitted,  
**WESTERMAN, HATTORI, DANIELS & ADRIAN, LLP**



Ryan B. Chirnomas  
Attorney for Applicants  
Registration No. 56,527  
Telephone: (202) 822-1100  
Facsimile: (202) 822-1111

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